REMARKS

The Office Action mailed January 26, 2004 has been received and reviewed. Claims 7 through 11 and 19 through 21 are identified as pending in the Office Action. Applicants have amended claims 7, 8, 9, 10, 11, 19 and 21 and added new claims 22 through 29. Reconsideration of the application as amended is respectfully requested.

Objection to the Specification

The specification was objected to in the Office action with respect to the language "on a PAAGE gel" in the paragraph beginning on line 4 of page 14 of the as-filed application. Applicants have amended this paragraph to recite "by SDS-PAGE" as suggested in the Office Action. Applicants note that PAAGE is an accepted abbreviation for "polyacrylamide gel electrophoresis" in Europe, which has the same meaning as "by SDS-PAGE." This amendment thus merely conforms the language to U.S. custom and does not alter the coverage or disclosure of the present application. It is requested the objection be withdrawn.

35 U.S.C. § 112, Second Paragraph, Rejection

Claim 21 was rejected as assertedly "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Office Action, at numbered paragraph 5, states that "it is unclear to what the applicant is referring" with respect to the language "comprises an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium" and inquires whether STMP is a strain of bacteria.

Applicants initially note that the assertedly indefinite language appears in both the Office Action at page 2 and the prior Office Action (mailed July 10, 2003) at page 3, which each state the present specification is "enabling for a vaccine composition for the protection against Salmonellosis comprising an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium and a pharmaceutical acceptable carrier, wherein the mutated bacterium lacking flagellin." Applicants have amended claim 21 to make it clear that *Salmonella typhimurium* STMP is a strain of

bacteria. Support for this amendment may be found at page 15, line 2 of the as-filed specification. It is requested this rejection be withdrawn.

35 U.S.C. § 112, First Paragraph, Rejections

Claims 7-11, 19 and 20 were rejected in the Office Action as assertedly lacking enablement under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse this rejection. It is noted that although the Office Action rejects claim 20 as assertedly lacking enablement in numbered paragraph 2, it states that this claim would be allowable if rewritten in independent form in numbered paragraph 4. Applicants respectfully submit that independent claims 7, 19 and 20 are enabled, as are the claims dependent therefrom.

The Office Action states that the specification while "enabling for a vaccine composition for the protection against Salmonellosis comprising an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium and a pharmaceutical acceptable carrier, wherein the mutated bacterium lacking flagellin does not reasonably provide enablement for a vaccine composition for the protection against Salmonellosis comprising an immunologically effective amount of any *Salmonella* mutated bacterium wherein the mutated bacterium lacking flagellin and wherein the mutated bacterium is attenuated." (Office Action at page 2, underlining in original).

In the previous amendment filed October 30, 2003, applicants explained that independent claims 7 and 19 are directed to a marker vaccine that allows exposure of an animal to a wild-type strain to be detected by antibody testing and that the present specification discloses and enables manufacture and use of such vaccines with multiple *Salmonella* strains. The present Office Action states the "claims are drawn to a vaccine composition" and the "term 'vaccine' encompasses the ability of the specific antigen to induce protective immunity to *Salmonella* infection or disease induction" (Office Action at page 3). It further states that the "claimed invention is not directed to a 'marker vaccine'" (Office Action at page 8). Based on these statements and a discussion of the cited references, it then concludes:

> One of skill in the art would not conclude that all strains of *Salmonella* encompassed by the claimed invention **are protective**

> based on the teaching of the prior art. Therefore, the specification is only enabled for vaccine compositions for the protection against Salmonellosis comprising an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium and a pharmaceutical acceptable carrier. (Office Action at page 8, underlining in original, emphasis added).

Applicants note that claims 7 and 19 were amended in the Amendment filed October 30, 2003 to remove the language "for the protection of animals against Salmonellosis" from the description of the respective vaccines and the enablement of these claims as directed to marker vaccines was discussed. Claims 7 and 19 are amended herein to make it clear they are directed to marker vaccines that allow exposure of an animal to a wild-type strain to be detected by antibody testing. The present specification discloses and enables manufacture and use of such marker vaccines with multiple *Salmonella* strains. Specifically, Example 3 of the specification demonstrates that two different vaccines strains, comprising STMP and STM2000, were able to reduce fecal shedding of a challenge strain significantly and that STMP and STM2000 inoculated chickens survived compared to an 80% death rate for those inoculated with a wildtype vaccine. Further, Example 4, at pages 22-23 of the specification, shows that live attenuated flagella-less *S. typhimurium* vaccine according to the invention give excellent results in pigs. Even more support is provided by Example 2, at page 18 of the specification, which discloses vaccines comprising flagellated and non-flagellated *Salmonellas,* specifically *S. entireditis* fla^+ and *S. entireditis* fla^-. The results of Example 2 show that *S. entireditis* fla^- vaccines also provide a clearly recognizable marker. The present specification thus teaches effective marker vaccines using *Salmonella* bacteria lacking flagellin, other than STM2000, and provides support for additional strains at page 6, lines 4-15 and page 9, lines 10-12. Accordingly, it is respectfully submitted that amended claim 7, with claims 8-11 dependent therefrom, and amended claim 19, are fully enabled.

Further, the Office Action again cites three references, Lockman et al., *Infection and Immunity*, Jan. 1990, p. 137-143 (hereinafter "Lockman"), Wahden et al., *Bull. World Health Organization*, vol. 52, 1975 (hereinafter "Wahdan"), and Hackett et al., *J. Infectious Diseases*, vol. 157, January 1988 (hereinafter "Hackett"). At pages 3 to 6, the Office Action examines each of

these references with respect to the characterization of flagella as virulence factors to state that the "role of attenuation to produce *Salmonella* nonflagelated mutants is unclear." (Office Action at page 6, underlining in original). From this examination, it is concluded that the "skilled artisan is forced into undue experimentation to practice (make and use) the invention as it is broadly claimed because the prior [art] has taught that many strains of fla$^-$ are not protective, do not confer protection from subsequent challenge by motile *Salmonella* bacteria and that mutations such as the flaF25 in the attenuation of Salmonella bacterium is unclear." (Office Action at page 6, underlining in original).

Lockman at page 137, right column, lines 3-7, discusses the paper by Hackett, stating "Nonflagellated strains colonized the intestinal tracts of orally vaccinated mice as well as isogenic flagellated strains yet did not confer equal protection from subsequent lethal challenge by motile *S. typhimurium* (18)." The cited publication, 18, is Hackett. Lockman further discusses this reference, stating that Hackett's flagella-less mutant has a "mutation that **not only** involves some of the genes encoding the biosynthesis of flagella, **but extended into a previously undescribed virulence gene(s)**." (*see,* Lockman at page 137, right column, lines 14-23). Similarly, Wahdan (although relating to *S. typhi* and *S. paratyphi A / B*, which are not claimed in the instant claims) acknowledges "[i]t seems more probable that a property other than the synthesis of the flagellar antigen determines immunogenicity and is absent from this non-motile motif." (Wahdan, p. 72, right column, last lines). Applicants thus respectfully submit that non-flagellin-related components of the non-mobile mutant lead to the lack of immunogenicity. Accordingly, these references are consistent with the present specification. Amended claims 7 and 19 are directed to effective marker vaccines using *Salmonella* bacteria lacking flagellin. *Salmonella* bacteria vaccine strains are used as a starting material, and used in a Fla$^-$ form. Accordingly, it is respectfully submitted that in view of these references, amended claim 7, with claims 8-11 dependent therefrom, and amended claim 19, are fully enabled by the present specification.

With respect to independent claim 20, the Office Action states the "specification has shown that the vaccines comprising mutated bacterium lacking flagellin from *S. typhimurium* STMP are protective. It is determine[d] that there are limited working examples commensurate in scope with the instant claims and that these is limited guidance provided in the specification as to how to make

and use vaccine compositions that comprise a mutated from any *Salmonella* bacterium (other than STM2000) lacking flagellin that are protective against Salmonellosis" (Office Action at page 2, underlining in original). The Office Action further states that "Applicant urges that Examples 3 and 4 of the instant specification show live attenuated flagella-less *S. typhimurium* vaccines, in contrast to Hackett et al, which teach that many fla-*Salmonella* stains [SIC] are not protective." (Office Action at page 7). The present specification, at Examples 3 and 4, shows that multiple flagella-less strains of *Salmonella typhimurium* provide protection in poultry and in pigs and claim 20 is directed only to "mutated *Salmonella typhimurium* bacterium" vaccines, not the multiple *Salmonella* species found in the other claims that were rejected under this blanket rejection. Accordingly, applicants respectfully submit that claim 20 is enabled and request it be allowed.

CONCLUSION

All pending claims are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact applicants' attorney.

Respectfully submitted,

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